REMARKS

Claims 1-8, 10-17 and 21-32 are allegedly finally rejected. Each remaining objection and rejection is addressed below. New claims 33-37 are added.

Claims are currently amended, notwithstanding Applicants' belief that the cancelled and unamended claims would have been allowable, without acquiescing to any of the Examiner's arguments, and without waiving the right to prosecute the unamended (or similar) claims in another application, but rather for the purpose of furthering Applicant's business goals and expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG).[1]

I. Specification: Redaction of Embedded Hyperlinks

In the Advisory Action mailed March 18, 2007, the Examiner states that previously requested amendments to replace www with "on the world wide web at" were not entered due to previous amendments submitted on Sept. 25, 2005 that deleted "http:". The Applicants again amend the Specification using the suggested replacement of "www." with "on the world wide web at" in order to be responsive to the Examiner's request for removal of embedded hyperlinks.

II. Title

In the Advisory Action mailed March 18, 2007, the Examiner states that the Title was not amended in response to the Examiner's statement that the Title was "not being descriptive of the elected invention." (Office Action mailed December 18, 2006, page 4). An amended title is suggested by the Applicants: "Novel Carotenoid ε- and β-Hydroxylases for use in engineering carotenoid metabolism in plants."

III. Written Description Rejections

In the Advisory Action mailed March 18, 2007, the Examiner states that Claims 1-8, 10-17 and 21-32 remain rejected "because the arguments are duplicative of those previously presented and already considered." Further, in the Office Action mailed

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[1] 65 Fed. Reg. 54603 (September 8, 2000).

December 18, 2006, wherein claims 1-8, 10-17 and 21-32 were rejected under 35 U.S.C. §112, first paragraph, pages 5-6, as allegedly failing to comply with the written description requirement, additionally referring to statements the Examiner made in Office Action mailed March 21, 2006, the Examiner states that Applicants argument that it serves no goal to have patentees recite known DNA sequences "is not persuasive because the instant claims encompass a large genus of molecules wherein only one is known in the art . . . . The only proven functional activity is the ability of SEQ ID NO:4 or 5 to complement the lut1 mutation in Arabidopsis. However, the specification does not describe any structural features that correspond to the functional activity of being able to complement the *lut1* mutation." (Office Action mailed March 21, 2006, page 5). The Applicants respectfully disagree.

In furtherance of the Applicants' assertion that the written description is adequate, the Applicants direct the Examiner's attention to the attached Declaration of Dr. Dean DellaPenna that demonstrates that a person of ordinary skill in the art[2] is able to make and identify a nucleic acid sequence encoding a polypeptide at least 78% identical to SEQ ID NO:4[3]. Specifically, Dr. DellaPenna states:

> The specification provides the structure for SEQ ID NO:4 and homologs such as rice CYP97C (LUT1; SEQ ID NO:16). The person of skill in the art would be able to make or identify nucleic acid sequences encoding proteins that are at least 72% identical to SEQ ID NO:4 (Figure 9). Many methods for making sequences with the requisite identity are taught in the specification, for example, at pages 51-64. The specification further teaches methods for screening for functional LUT1 sequences by complementation of LUT1 mutants in Examples 3 and 5. This structural information and the screening procedures allows the person of skill in the art to identify a genus of nucleic acid sequences encoding proteins at least 72% identical to SEQ ID NO:4 that have functional LUT1 activity as claimed.

The Examiner's attention is respectfully directed to the Federal Circuit's recent holding in Falkner v. Inglis, 448 F.3d 1357; 79 U.S.P.Q.2D (BNA) 1001 (Fed. Cir. 2006) showing that the disclosures of the present inventions meet and exceed present relative case law. In Falkner, the Federal Circuit explained that "[t]he 'written description'

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2 See, "Declaration Pursuant To 37 C.F.R. 1.132", paragraph 2.

3 Id, at paragraphs 2 and 3.

requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution." Id. at 1358. As held by the Federal Circuit in Falkner, "Since the law is applied to each invention in view of the state of relevant knowledge, its application will vary with differences in the state of knowledge in the field and differences in the predictability of the science." Falkner, 448 F.3d at 1367-68. Dr. DellaPenna provides evidence that a person of skill in the art would recognize that the inventors were in possession claimed sequences based on the discosure of the specification.

Moreover, Dr. DellaPenna describes a publication[4] wherein an Arabidopsis CYP97C (LUT1) sequence was used to identify a CYP97C homolog in Oryza sativa (rice). Moreover, at the time of filing of the present inventions, the Applicant's had already used Arabidopsis CYP97C (LUT1) to identify the rice homolog of SEQ ID NO:4, shown as SEQ ID NO:16 in Figure 23, with 78% homology to SEQ ID NO:4, *See*, Figure 9 of the instant application. Further demonstrating that rice CYP97C (LUT1) nucleotides were indeed identified at the time of filing the present application.

Furthermore, the Applicants used structural features of SEQ ID NO:4, specifically including p450 activity, and targeting sequences, to identify a large genus of p450 molecules, such as CYP97C sequences encoding homologous SEQ ID NO:4 LUT1 proteins, CYP97A sequences encoding proteins at least 49% identical to SEQ ID NO:4[5], and CYP97B sequences encoding proteins at least 42% identical to SEQ ID NO:4[6], where examples of such molecules are shown in Figures 5, 8 and 11. (*See also*, Application as published, EXAMPLES 2-4). Moreover, structural features identified and described for LUT1 allowed the Applicants to further identify known LUT1 homologs in a range of species, (*See*, Application as published, EXAMPLE 6 and Figure 5). The applicants' further point to Figure 10 of the present inventions showing one example of how specific internal structural features of the disclosed Arabidopsis LUT1 SEQ ID

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4 Quinlan *et al.*, Escherichia coli as a platform for functional expression of plant P450 carotene hydroxylases, Archives of Biochemistry and Biophysics 458 (2007) 146–157.

5 See, published application, page 37, Example 6, paragraph [0342].

6 Id.

NO:04 was used to identify a larger genus of molecules, including CYP97A, CYP97B, and CYP97C. Therefore the Application indeed teaches the LUT1 SEQ ID NO:4 in addition to a larger genus of molecules, specifically CYP97A, CYP97B and CYP97C p450 families, which itself structural information plainly understood and used by a person of ordinary skill in the art at the time of filing of the present inventions.

Therefore, it is beyond doubt that as of the filing date of the instant invention, a person of ordinary skill in the art could make and identify nucleic acid sequences encoding a polypeptide at least 72% identical to SEQ ID NO:4 whose structural information can be and was used to identify a large genus of molecules having monooxygenase P450 activity, CYP97A, CYP97B and CYP97C families. Furthermore, that person could and did use such sequences to make vectors and transgenic organisms as described in the specification.

Thus the written description requirements was met. Accordingly, the Applicants respectfully request these rejections be withdrawn.

IV. Enablement Rejections

In the Advisory Action mailed March 18, 2007, the Examiner states that Claims 1-8, 10-15, 21-32, and amended Claims 16 and 17 remain rejected "because the arguments are duplicative of those previously presented and already considered." Further, in the Office Action mailed December 18, 2006, wherein Claims 1-8, 10-15, 21-32, were rejected under 35 U.S.C. §112, first paragraph, pages 5-6, as allegedly failing to comply with the enablement requirement, the Examiner continues to refer to statements/arguments the Examiner made in the Office Action mailed March 21, 2006. In particular, the Examiner states, " . . . one of skill in the art would not know how to use the nucleic acids and vectors for prokaryotic or yeast expression (claims 11 and 14 are specifically not enabled for these reasons)." (Office Action mailed March 21, 2006, pages 7-11). Further, in the Office Action mailed December 18, 2007, the examiner invited the Applicants to "submit evidence in the form of data/declaration under 37 C.F.R. 1.132 showing that a nucleic acid encoding SEQ ID NO:04 can be successfully expressed in yeast or E. Coli . . .. " The Applicants herein submit a declaration by the

inventor[7] who is "one of skill in the art" describing a recent publication that demonstrated expression of a rice homolog of LUT1 in E. Coli[8]. Furthermore Quinlan *et al.*, showed that E. coli that expressed a rice CYP97C (LUT1) homolog were shown to increase production of molecules with ε-ring hydroxylation in contrast to E. coli not expressing the rice CYP97C sequence. Thus the Applicants respectfully assert that the enablement requirement has been met.

The Applicants further point out that the invention as claimed is enabled, for example, by describing a prokaryotic vector (pMLBART vector (Gleave, Plant Mol. Biol. 20, 1203-1207 (1992), see paragraph [0327] of the published application) and a yeast expression vector comprising a LUT1 cDNA, see, Figure 12 of the present application. Thus the Applicants believe that Claims 11 and 14 are enabled. Moreover, the Tian paper cited by the Examiner merely indicates that initial attempts at expression in yeast were unsuccessful. There is no evidence that use of other methods known in the art and methods and constructs described in the specification would be unsuccessful. Applicants further note that even though the Tian paper published after the filing data of the present application, it was submitted on a date before the present application was filed.

Further, the Examiner states: "it would require undue experimentation on the part of one skilled in the art to determine the results of expression SEQ ID NO:05 in a plant, and to elucidate what other steps (if any) would be required to generate a useful plant . . .. one of skill in the art would not know how to use the claimed expression vectors, nucleic acids, transgenic plants and seeds, and the methods recited in claims 28-32 are not enabled." (Office Action mailed March 21, 2006, page 10). The Applicants respectfully disagree. In particular, the invention as claimed is enabled, for example, by describing plants transgenically expressing SEQ ID NO:05. (*See*, Application as published, paragraph [0155]). Again, as held by the Federal Circuit in Falkner, "Since the law is applied to each invention in view of the state of relevant knowledge, its application will vary with differences in the state of knowledge in the field and differences in the

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7 See, "Declaration Pursuant To 37 C.F.R. 1.132", paragraph 2.

8 Quinlan *et al.*, Escherichia coli as a platform for functional expression of plant P450 carotene hydroxylases, Archives of Biochemistry and Biophysics 458 (2007) 146–157.

predictability of the science." Falkner, 448 F.3d at 1367-68. The Examiner has provided no evidence that the current invention was unpredictable as of the filing date of the invention. Instead, the Examiner has relied on outdated papers published in 1993 and 1998. Applicants respectfully submit that the claimed inventions were enabled as of the filing date of the present application.

Accordingly, the Applicants respectfully request these rejections for Claims 1-8, 10-15 and 21-32 be withdrawn.

CONCLUSION

The Applicant believes the arguments set forth above traverse the Examiner's objections and rejections and therefore request these alleged grounds for objection and rejection be withdrawn. Should the Examiner believe a telephone interview would aid in the prosecution of this application, the Applicant encourages the Examiner to call the undersigned collect.

Dated: May 18, 2007

J. Mitchell Jones, J.D., Ph.D.
Registration No. 44,174

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
415.904.6500

PATENT
Attorney Docket No. **MSU-08604**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Dean DellaPenna *et al.*
Serial No.: 10/751,235 Group No.: 1638
Filed: 01/02/2004 Examiner: Worley, C.K.
Entitled: **Novel Carotenoid Hydroxylases For Use In Engineering Carotenoid Metabolism In Plants**

DECLARATION OF DR. DEAN DELLAPENNA PURSUANT TO 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: May 18, 2007 By: _____

I, Dr. Dean DellaPenna, state that:

1. I am a joint inventor of the subject matter claimed in the above captioned United States Patent Application. I am a Professor in the Department of Biochemistry and Molecular Biology at Michigan State University.

2. It is my understanding that the examiner has rejected claims to vectors and the use of nucleic acid sequences encoding proteins with greater than 80% identity to LUT1 (i.e., SEQ ID NO:4). In particular, the Examiner has alleged that the specification does not describe any structural features that correspond to the functional activity of being able to complement the *lut1* mutation and does not provide support for the genus of nucleic acid sequences encoding proteins that are at least 80% identical to SEQ ID NO:4.

I do not agree with the Examiner's allegations. One example of "one of skill in the art" in the field of plant genetics and molecular biology is a person with about 2 to 4 years of post-doctoral research experience. My experience exceeds this example. The specification provides the structure for SEQ ID NO:4 and homologs such as rice CYP97C (LUT1; SEQ ID NO:16). The person of skill in the art would be able to make or identify nucleic acid sequences encoding proteins that are at least 72% identical to SEQ ID NO:4 (Figure 9). Many methods for making sequences with the requisite identity are taught in the specification, for example, at pages 51-64. The specification further teaches methods for screening for functional LUT1 sequences by complementation of LUT1 mutants in Examples 3 and 5. This structural information and the screening procedures allows the person of skill in the art to identify a genus of nucleic acid sequences encoding proteins at least 72% identical to SEQ ID NO:4 that have functional LUT1 activity as claimed.

3. It is also my understanding that the Examiner's position is that one of skill in the art would not know how to use the claimed nucleic acids and vectors for prokaryotic or yeast expression. This is not a scientifically valid argument. A person of ordinary skill in the art, as defined above, would be able to express the claimed sequences in bacteria or yeast using the methods taught in the present application or otherwise known in the art. For example, Quinlan *et al.*, used Escherichia coli as a platform for functional expression of plant P450 carotene hydroxylases, Archives of Biochemistry and Biophysics 458 (2007) 146–157, have recently described the transfection of a prokaryotic expression vector comprising a CYP97C (LUT1) nucleic acid coding sequence into bacteria for expressing a plant ε-ring hydroxylase. Specifically, Quinlan *et al.*, used an Arabidopsis CYP97C (LUT1) of the present invention (SEQ ID NO:04) coding sequence to obtain a Oryza sativa (rice) LUT1 homolog (GenBank #AK065689). As stated in the patent, the Arabidopsis gene sequence (SEQ ID NO:05) was used by a person of ordinary skill in the art to identify this related rice gene. This paper further demonstrated that expression of the rice LUT1 homolog resulted in a change in carotenoid production from the bacteria expressing rice LUT1 relative to both bacteria transformed with a β-hydroxylase coding sequence and bacteria transformed with a control vector. In

particular, bacteria that expressed plant ε-ring hydroxylase showed a loss of a lutein precursor lycopene (φ, φ -carotene) associated with a gain of ε, φ - carotene product (δ-carotene) and ε, ε -carotene product (lactucaxanthin). Furthermore the Oryza sativa (rice) LUT1 homolog (GenBank #AK065689) nucleic acid homolog (SEQ ID NO:22 and amino acid sequence SEQ ID NO:16) was disclosed in the present application. Moreover, Arabidopsis LUT1 (SEQ ID NO:04) disclosed in the present inventions was described in the instant application as showing 78% amino acid sequence homology to Oryza sativa (rice) LUT1 amino acid homolog encoded by a nucleic acid sequence located at GenBank #AK065689 (SEQ ID NO:16) (Figures 9 and 23). This shows that sequences with the requisite identity function as claimed and that persons of ordinary skill in the art would be able to use the sequences as claimed.

4. I further declare that all statement made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: May 18, 2007

Dr. Dean DellaPenna